REMARKS

Status of the Claims

Claims 1, 2 and 5-18 are pending in the application. Of these, claims 6-18 were withdrawn from consideration. Claims 1, 2 and 5 are rejected.

Withdrawn claims 6-18 are canceled herein. Claim 1 is amended. Claim 2 is canceled. Claim 5 is not amended.

Claim Amendments

Claim 2 is canceled. Claim 1 is amended so that the subject matter claimed in this claim would be commensurate with the scope of the invention disclosed in the specification.

Amended claim 1 is directed to a method of treating uterine serous papillary carcinoma that over-express HER-2/neu, comprising the step of administering to an individual with the carcinoma a therapeutically effective dose of humanized murine anti-HER-2/neu monoclonal antibody 4D5 that binds to the extracellular domain of HER-2/neu.

In the Advisory Action mailed October 22, 2004, the Examiner states that the claim amendments made in response to the Final Office Action were not entered since the newly amended claim raised 35 U.S.C. §112, first and second paragraph issue. The 35 U.S.C. §112, first paragraph issue was raised by the Examiner because the amended claim recited monoclonal antibody 4D5, which had not been deposited by the Applicants. The 35 U.S.C. §112, second paragraph issue was raised due to the recitation of Herceptin, which is a trademark in the amended claim and, according to the Examiner, the scope of the claim was uncertain since the trademark or trade name cannot be used to properly identify any particular material of product.

In response to the issue of whether a deposit of monoclonal antibody 4D5 would be required under the patent laws, Applicants would like to respectfully point out that specification explicitly teaches that the humanized murine anti-HER-2/neu monoclonal antibody (MAb) 4D5 is HERCEPTIN®, which has been reported to have therapeutic effects in patients with breast carcinomas, when combined with other chemotherapeutic drugs

(amendments to specification, paragraph beginning on page 4, line 6, mailed December 11, 2003). Additionally, the specification also states that this antibody was obtained from Genentech, San Francisco, CA (amendments to specification, paragraph beginning on page 18, line 5, mailed December 11, 2003). Therefore, this antibody is well known and commercially available to the public. Accordingly, no deposit is necessary.

Further, in response to the objection by the Examiner regarindg the incorporation of the trademark HERCEPTIN® in the claim, Applicants have deleted the trademark recitation from the claim as it is unnecessary to describe this antibody. Hence, in view of these amendments, Applicants submit that the claim amendments address the objections raised by the Examiner. Accordingly, Applicants respectfully request the Examiner to enter the proposed claim amendments and withdraw the rejections of independent claim 1 and dependent claim 5 under 35 U.S.C §112, first paragraph.

Applicants also respond to the 35 U.S.C. §112, first paragraph rejection of claim 2 in the Final Office Action, mailed March 2, 2004. Claim 2 stands rejected for failing to provide an

adequate written description of the invention and failing to provide an enabling disclosure, because the specification did not provide evidence that the claimed biological materials are (1) known and readily available to the public, (2) reproducible from a written description (e.g. sequenced); or (3) deposited.

Claim 2 has been canceled. Therefore, 35 U.S.C. §112, first paragraph rejection of this claim is moot.

Additionally, Applicants respond to the 35 U.S.C. §103(a) rejection of claims 1, 2 and 5 that remain rejected for reasons previously set forth in the paper mailed November 5, 2003, section 10, pages 14-17. Applicants respectfully traverse this rejection.

In the Advisory action, the Examiner states that the Applicants' arguments regarding teachings of **Bookman** *et al,* **(J. Clinical Oncology, 21:283-290), Berchuck** *et al.*, **Saffari** *et al.* and **Wang** *et al.* made in the Response after Final were unpersuasive. The Examiner states that in addition to above combination of cited prior art references, Applicants had not addressed issues raised due to inclusion of **Baselga** *et al.*, **Agus** *et*

al and **Pegram** *et al* in this combination. Further, the Examiner contended that Applicants argued the references individually without clearly addressing the combined teachings. Based on the teachings of prior art, the Examiner states that it would have been obvious, as set forth in the first action on merits, to treat subset of uterine serous papillary carcinoma with HERCEPTIN® with reasonable expectation of success. Applicants respectfully disagree.

The instant invention is directed to a method of treating Her-2/neu over-expressing uterine serous papillary carcinoma with humanized murine anti-HER-2/neu monoclonal antibody 4D5. **Baselga** *et al* teach the use of anti-Her-2/neu antibody, monoclonal antibody 4D5 in the treatment of Her-2-over-expressing metastatic cancer but do not teach or suggest the use of this antibody in treating uterine serous papillary carcinoma. **Agus** *et al* examine treatment of epithelial cancers such as lung, ovarian and prostrate cancers with anti-Her-2/neu antibody (HERCEPTIN®) alone or in combination with chemotherapy. **Pegram** *et al* teach that the use of recombinant human (rhu) anti-Her-2 monoclonal antibody in combination with cisplatin in patients with Her-2/neu-over-expressing metastatic breast

cancer resulted in objective clinical response rates higher than those reported previously for cisplatin alone or rhu anti-Her-2 monoclonal antibody alone. **Berchuck** *et al* analyzed 12 papillary carcinoma samples out of 95 samples and reported high Her-2/neu staining in 3 samples (page 17, column 2, last paragraph). **Saffari** *et al* reported that of the three uterine serous papillary carcinoma cases that were examined, only one showed high Her-2/neu expression, while there was low Her-2/neu expression in the other two samples (page 5964, Table 1). **Wang** *et al* reported Her-2/neu expression in one sample with uterine papillary serous carcinoma and both Her-2/neu and epidermal growth factor receptor expression in the other sample with uterine papillary serous carcinoma. **Bookman** *et al* evaluated the feasibility, toxicity and efficacy of single agent HERCEPTIN® in patients with recurrent or persistent ovarian or primary peritoneal carcinoma. Of the 41 patients that were treated, only 3 achieved an objective response. Of these 3 patients, only one had a complete response while the other two had a partial response.

Thus, if a person having ordinary skill in this art were to combine the teachings of prior art directed to the expression of Her-

2/neu in cancer with those directed to use of HERCEPTIN® in treating such cancers, a person having ordinary skill in this art would never arrive at the claimed invention. Specifically, since the cited prior art references such as **Pegram** *et al* directed to the use of HERCEPTIN® teach that objective clinical rates with a combination of rhu anti-Her-2 monoclonal antibody and cisplatin was much higher than either used singly. Similarly, the prior art reference, **Bookman** *et al* explicitly state that based on low frequency of Her-2/neu over-expression and very low response rates to single agent HERCEPTIN®, it would be practical to combine HERCEPTIN® with platinum based therapy. Furthermore, **Bookman** *et al* suggest targeting other related signal transduction molecules to increase the proportion of patients that might benefit from a combined therapy approach (page 289, column 2, last paragraph). Hence by teaching against the use of HERCEPTIN® alone in treatment of cancer, the combined teaching of the cited prior art references teach away from the instant invention. Despite the lack of teaching in the prior art regarding success in using HERCEPTIN® alone, if one of ordinary skill in the art were motivated to treat Her-2/neu over-expressing uterine serous papillary carcinoma with HERCEPTIN® as claimed in the instant invention, there would be no

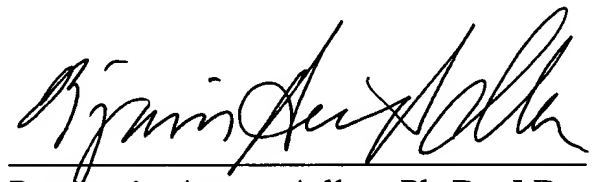
reasonable expectation of success and one would be merely trying to arrive at the claimed invention. It has long been established that merely "trying" is not a standard for obviousness under 35 U.S.C. §103.

Applicants assert that obviousness requires that the prior art relied upon fairly teach or suggest all the elements of the instant invention and that an incentive or motivation be present in the prior art to produce the claimed invention with reasonable expectation of success in its production. The Applicants have shown that **cited prior art references** combined do not teach or suggest all the elements of the present invention, nor do they provide an incentive or motivation to produce the claimed invention with reasonable expectation of success in its production. Hence, the subject matter of the present invention is not obvious to one with ordinary skill in the art at the time the invention was made. Accordingly, based on the above-mentioned remarks, amendment and cancellation of claim 2, Applicants respectfully request that the rejection of claims 1-2 and 5 under 35 U.S.C. §103 be withdrawn.

This is intended to be a complete response to the Advisory Action, mailed October 22, 2004 and to the Final Office Action, mailed March 2, 2004. Applicants submit that the pending claims are in condition for allowance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: 11/17/04



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